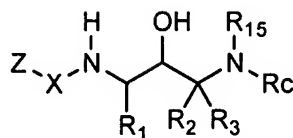


Claim 1. (currently amended) A compound of the formula ~~(I)~~:



~~(I)~~

or a pharmaceutically acceptable salt or ester thereof,
 wherein Z is aryl, heteroaryl or heterocyclyl, wherein said groups are optionally substituted with 1 or 2 R_B groups, wherein,
 where R_B at each occurrence is independently selected from halogen, -OH, -OCF₃, -O-phenyl, -CN, -NR₁₀₀R₁₀₁, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, (CH₂)₀₋₃(C₃-C₇ cycloalkyl), aryl, heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, halogen, -OH, -CN, or -NR₁₀₀R₁₀₁;

where R₁₀₀ and R₁₀₁ are at each occurrence are independently H, C₁-C₆ alkyl, or phenyl;

X is -(C=O)- or -(SO₂)-;

wherein R₁ is C₁-C₁₀ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, =O, -SH, -CN, -CF₃, -OCF₃, -C₃₋₇ cycloalkyl, -C₁-C₄ alkoxy, amino, mono-dialkylamino, aryl, heteroaryl, heterocycloalkyl, wherein each aryl group is optionally substituted with 1, 2 or 3 R₅₀ groups;

wherein R_{50} is selected from halogen, OH, SH, CN, $-\text{CO}-(\text{C}_1-\text{C}_4 \text{ alkyl})$, $-\text{NR}_7\text{R}_8$, $-\text{S}(\text{O})_{0-2}-(\text{C}_1-\text{C}_4 \text{ alkyl})$, $\text{C}_1-\text{C}_6 \text{ alkyl}$, $\text{C}_2-\text{C}_6 \text{ alkenyl}$, $\text{C}_2-\text{C}_6 \text{ alkynyl}$, $\text{C}_1-\text{C}_6 \text{ alkoxy}$ and $\text{C}_3-\text{C}_8 \text{ cycloalkyl}$;

wherein the alkyl, alkenyl, alkynyl, alkoxy and cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of $\text{C}_1-\text{C}_4 \text{ alkyl}$, halogen, OH, $-\text{NR}_5\text{R}_6$, CN, $\text{C}_1-\text{C}_4 \text{ haloalkoxy}$, NR_7R_8 , and $\text{C}_1-\text{C}_4 \text{ alkoxy}$;

wherein R_5 and R_6 are independently H or $\text{C}_1-\text{C}_6 \text{ alkyl}$; or

wherein R_5 and R_6 and the nitrogen to which they are attached form a 5 or 6 membered heterocycloalkyl ring; and

wherein R_7 and R_8 are independently selected from the group consisting of H; $-\text{C}_1-\text{C}_4 \text{ alkyl}$ optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of $-\text{OH}$, $-\text{NH}_2$, and halogen; $-\text{C}_3-\text{C}_6 \text{ cycloalkyl}$; $-(\text{C}_1-\text{C}_4 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_4 \text{ alkyl})$; $-\text{C}_2-\text{C}_4 \text{ alkenyl}$; and $-\text{C}_2-\text{C}_4 \text{ alkynyl}$;

wherein each heteroaryl is optionally substituted with 1 or 2 R_{50} groups;

wherein each heterocycloalkyl group is optionally substituted with 1 or 2 groups that are independently R_{50} or $=\text{O}$;

R₂ and R₃ are independently selected from

-H;

-F;

-C₁-C₆ alkyl optionally substituted with a substituent selected from the group consisting of -F, -OH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR₅R₆;

-(CH₂)₀₋₂-R₁₇;

-(CH₂)₀₋₂-R₁₈;

-C₂-C₆ alkenyl or C₂-C₆ alkynyl, wherein each is optionally substituted with an independent substituent selected from the group consisting of -F, -OH, -C≡N, -CF₃ and C₁-C₃ alkoxy;

-(CH₂)₀₋₂-C₃-C₇ cycloalkyl, optionally substituted an independent substituent selected from the group consisting of -F, -OH, -C≡N, -CF₃, C₁-C₃ alkoxy and -NR₅R₆; or

R₂, R₃ and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one carbon atom is optionally replaced by a group selected from -O-, -S-, -SO₂-, or -NR₇-;

where R₁₇ at each occurrence is an aryl group selected from phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl and tetralinyl, wherein said aryl groups are optionally substituted with one or two groups that are independently

-C₁-C₃ alkyl; -C₁-C₄ alkoxy; CF₃; or

-C₂-C₆ alkenyl or -C₂-C₆ alkynyl each of which is optionally substituted with one substituent selected from the group consisting of F, OH, C₁-C₃ alkoxy; or
-halogen;
-OH;
-C≡N;
-C₃-C₇ cycloalkyl;
-CO-(C₁-C₄ alkyl);
-SO₂-(C₁-C₄ alkyl);

where R₁₈ is a heteroaryl group selected from pyridinyl, pyrimidinyl, quinolinyl, indolyl, pyridazinyl, pyrazinyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, oxazolyl, thiazolyl, furanyl, thienyl, pyrrolyl, oxadiazolyl or thiadiazolyl, wherein each of said heteroaryl groups is optionally substituted with one or two groups that are independently

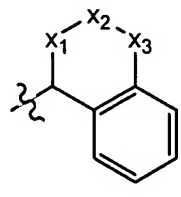
-C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of OH, C≡N, CF₃, C₁-C₃ alkoxy, and -NR₅R₆;

R₁₅ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, hydroxy C₁-C₆ alkyl, halo C₁-C₆ alkyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, C₁-C₆ alkyl, hydroxy, C₁-C₆ alkoxy, NH₂, and -R₂₆-R₂₇;

wherein R_{26} is selected from the group consisting of a bond, $-C(O)-$, $-SO_2-$, $-CO_2-$, $-C(O)NR_5-$, and $-NR_5C(O)-$,

wherein R_{27} is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, aryl C_1-C_6 alkyl, heterocycloalkyl, and heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, haloalkyl, hydroxyalkyl, $-NR_5R_6$, $-C(O)NR_5R_6$;

R_c is a group of the formula



wherein x_1 , x_2 , and x_3 are independently $-CHR_{245}$, SO_2 , or NH , and
wherein the phenyl ring is optionally substituted with 1 or 2 -
 R_{245} groups,

~~selected from the group consisting of~~

~~$-(CH_2)_{0-3}-(C_3-C_8)$ cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of $-R_{205}$, $-CO_2-(C_1-C_4)$ alkyl, and aryl, wherein aryl is optionally substituted with 1 or 2 independently selected R_{200} groups;~~

~~$-(CR_{245}R_{250})_{0-4}$ aryl;~~

~~$-(CR_{245}R_{250})_{0-4}$ heteroaryl;~~

~~$-(CR_{245}R_{250})_{0-4}$ heterocycloalkyl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-aryl-heteroaryl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-aryl-heterocycloalkyl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-aryl-aryl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-heteroaryl-aryl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-heteroaryl-heterocycloalkyl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-heteroaryl-heteroaryl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-heterocycloalkyl-heteroaryl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-heterocycloalkyl-heterocycloalkyl;~~

~~-(CR₂₄₅R₂₅₀)₀₋₄-heterocycloalkyl-aryl;~~

~~a monocyclic or bicyclic ring of 5, 6, 7, 8, 9, or 10 carbons fused to 1 or 2 aryl, heteroaryl, or heterocycloalkyl groups wherein 1, 2 or 3 carbons of the monocyclic or bicyclic ring is optionally replaced with~~

~~—NH—~~

~~—N(CO)₀₋₁R₂₁₅—~~

~~—N(CO)₀₋₁R₂₂₀—~~

~~—O— or~~

~~—S(=O)₀₋₂—~~

~~and wherein the monocyclic or bicyclic ring is optionally substituted with 1, 2 or 3 groups that are independently~~

~~R₂₀₅, R₂₄₅, R₂₅₀ or =O;~~

~~C₂-C₆-alkenyl optionally substituted with 1, 2, or 3 R₂₀₅ groups;~~

~~C₂-C₆-alkynyl optionally substituted with 1, 2, or 3 R₂₀₅ groups;~~

~~wherein each aryl group attached directly or indirectly to the $(\text{CR}_{245}\text{R}_{250})_{0-4}$ group is optionally substituted with 1, 2, 3 or 4 R_{200} groups;~~

~~wherein each heteroaryl group attached directly or indirectly to the $(\text{CR}_{245}\text{R}_{250})_{0-4}$ group is optionally substituted with 1, 2, 3, or 4 R_{200} ;~~

~~wherein each heterocycloalkyl attached directly or indirectly to the $(\text{CR}_{245}\text{R}_{250})_{0-4}$ group is optionally substituted with 1, 2, 3, or 4 R_{210} ;~~

~~wherein R_{200} at each occurrence is independently selected from the group consisting of~~

~~$\text{C}_1\text{-C}_6$ alkyl optionally substituted with 1, 2, or 3 R_{205} groups;~~

~~-OH ;~~

~~-NO_2 ;~~

~~halogen;~~

~~$\text{-C}\equiv\text{N}$;~~

~~$(\text{CH}_2)_{0-4}\text{-CO-NR}_{220}\text{R}_{225}$;~~

~~$(\text{CH}_2)_{0-4}\text{-CO-(C}_1\text{-C}_8\text{ alkyl)}$;~~

~~$(\text{CH}_2)_{0-4}\text{-CO-(C}_2\text{-C}_8\text{ alkenyl)}$;~~

~~$(\text{CH}_2)_{0-4}\text{-CO-(C}_2\text{-C}_8\text{ alkynyl)}$;~~

~~$(\text{CH}_2)_{0-4}\text{-CO-(C}_3\text{-C}_7\text{ cycloalkyl)}$;~~

~~$(\text{CH}_2)_{0-4}\text{-(CO)}_{0-1}\text{-aryl}$;~~

~~$(\text{CH}_2)_{0-4}\text{-(CO)}_{0-1}\text{-heteroaryl}$;~~

~~$(\text{CH}_2)_{0-4}\text{-(CO)}_{0-1}\text{-heterocycloalkyl}$;~~

~~$(\text{CH}_2)_{0-4}\text{-CO}_2\text{R}_{215}$;~~

~~—(CH₂)₀₋₄—SO₂—NR₂₂₀R₂₂₅†~~

~~—(CH₂)₀₋₄—S(O)₀₋₂—(C₁–C₈ alkyl)†~~

~~—(CH₂)₀₋₄—S(O)₀₋₂—(C₃–C₇ cycloalkyl)†~~

~~—(CH₂)₀₋₄—N(H or R₂₁₅)—CO₂R₂₁₅†~~

~~—(CH₂)₀₋₄—N(H or R₂₁₅)—SO₂—R₂₂₀†~~

~~—(CH₂)₀₋₄—N(H or R₂₁₅)—CO—N(R₂₁₅)₂†~~

~~—(CH₂)₀₋₄—N(H or R₂₁₅)—CO—R₂₂₀†~~

~~—(CH₂)₀₋₄—NR₂₂₀R₂₂₅†~~

~~—(CH₂)₀₋₄—O—CO—(C₁–C₆ alkyl)†~~

~~—(CH₂)₀₋₄—O—(R₂₁₅)†~~

~~—(CH₂)₀₋₄—S—(R₂₁₅)†~~

~~—(CH₂)₀₋₄—O—(C₁–C₆ alkyl optionally substituted with 1, 2, 3, or 5 —F)†~~

~~—C₂–C₆ alkenyl optionally substituted with 1 or 2 R₂₀₅ groups†~~

~~—C₂–C₆ alkynyl optionally substituted with 1 or 2 R₂₀₅ groups†~~

~~—and~~

~~—(CH₂)₀₋₄—C₃–C₇ cycloalkyl†~~

~~—wherein each aryl group included within R₂₀₀ is optionally substituted with 1, 2, or 3 groups that are independently~~

~~—R₂₀₅†~~

~~—R₂₁₀ or~~

~~—C₁–C₆ alkyl substituted with 1, 2, or 3 groups that are independently R₂₀₅ or R₂₁₀†~~

~~wherein each heterocycloalkyl group included within R_{200} is optionally substituted with 1, 2, or 3 groups that are independently R_{210}~~

~~wherein each heteroaryl group included within R_{200} is optionally substituted with 1, 2, or 3 groups that are independently~~

~~_____ R_{205}~~

~~_____ R_{210} or~~

~~_____ C_1-C_6 alkyl substituted with 1, 2, or 3 groups that are independently~~

~~_____ R_{205} or~~

~~_____ R_{210}~~

~~wherein R_{205} at each occurrence is independently selected from the group consisting of~~

~~_____ C_1-C_6 alkyl,~~

~~_____ C_2-C_6 alkenyl,~~

~~_____ C_2-C_6 alkynyl,~~

~~_____ C_1-C_6 haloalkoxy~~

~~_____ $(CH_2)_{0-3}(C_3-C_7$ cycloalkyl)~~

~~_____ halogen,~~

~~_____ $(CH_2)_{0-6}OH$,~~

~~_____ O phenyl,~~

~~_____ SH ,~~

~~_____ $(CH_2)_{0-6}C\equiv N$,~~

~~(CH₂)₀₋₆-C(=O)NR₂₃₅R₂₄₀~~

~~CF₃~~

~~C₁-C₆ alkoxy, and~~

~~NR₂₃₅R₂₄₀~~

wherein ~~R₂₁₀~~ at each occurrence is
independently selected from the group
consisting of

~~C₁-C₆ alkyl optionally substituted with 1, 2, or
3 R₂₀₅ groups;~~

~~C₂-C₆ alkenyl optionally substituted with 1, 2,
or 3 R₂₀₅ groups;~~

~~C₂-C₆ alkynyl optionally substituted with 1, 2,
or 3 R₂₀₅ groups;~~

~~halogen;~~

~~C₁-C₆ alkoxy;~~

~~C₁-C₆ haloalkoxy;~~

~~NR₂₂₀R₂₂₅;~~

~~OH;~~

~~C≡N;~~

~~C₃-C₇ cycloalkyl optionally substituted with 1,
2, or 3 R₂₀₅ groups;~~

~~CO-(C₁-C₄ alkyl);~~

~~SO₂NR₂₃₅R₂₄₀;~~

~~CO-NR₂₃₅R₂₄₀;~~

~~SO₂-(C₁-C₄ alkyl); and~~

~~_____ =O; wherein~~

~~wherein R₂₁₅ at each occurrence is independently selected from the group consisting of~~

~~_____ C₁-C₆ alkyl,~~

~~_____ (CH₂)₀₋₂ (aryl),~~

~~_____ C₂-C₆ alkenyl,~~

~~_____ C₂-C₆ alkynyl,~~

~~_____ C₃-C₇ cycloalkyl,~~

~~_____ (CH₂)₀₋₂ (heteroaryl), and~~

~~_____ (CH₂)₀₋₂ (heterocycloalkyl);~~

~~wherein the aryl group included within R₂₁₅ is optionally substituted with 1, 2, or 3 groups that are independently~~

~~_____ R₂₀₅ or~~

~~_____ R₂₁₀;~~

~~wherein the heterocycloalkyl group included within R₂₁₅ is optionally substituted with 1, 2, or 3 R₂₁₀;~~

~~wherein each heteroaryl group included within R₂₁₅ is optionally substituted with 1, 2, or 3 R₂₁₀;~~

~~wherein R₂₂₀ and R₂₂₅ at each occurrence are independently selected from the group consisting of~~

~~_____ H,~~

~~_____ C₁-C₆ alkyl,~~

~~_____ hydroxy C₁-C₆ alkyl,~~

~~_____ amino C₁-C₆ alkyl,~~

~~_____ halo C₁-C₆ alkyl,~~

~~_____ (CH₂)₀₋₂ (C₃-C₇ cycloalkyl),~~

~~— (C₁-C₆ alkyl) O (C₁-C₃ alkyl),~~

~~— C₂-C₆ alkenyl,~~

~~— C₂-C₆ alkynyl,~~

~~— aryl,~~

~~— heteroaryl, and~~

~~— heterocycloalkyl,~~

~~wherein the aryl, heteroaryl or heterocycloalkyl group included within R₂₂₀ and R₂₂₅ is optionally substituted with 1, 2, or 3 R₂₇₀ groups,~~

~~wherein R₂₇₀ at each occurrence is independently~~

~~— R₂₀₅,~~

~~— C₁-C₆ alkyl optionally substituted with 1, 2, or 3 R₂₀₅ groups,~~

~~— C₂-C₆ alkenyl optionally substituted with 1, 2, or 3 R₂₀₅ groups,~~

~~— C₂-C₆ alkynyl optionally substituted with 1, 2, or 3 R₂₀₅ groups,~~

~~— halogen,~~

~~— C₁-C₆ alkoxy,~~

~~— C₁-C₆ haloalkoxy,~~

~~— NR₂₃₅R₂₄₀,~~

~~— OH,~~

~~— C≡N,~~

~~— C₃-C₇ cycloalkyl optionally substituted with 1, 2, or 3 R₂₀₅ groups,~~

~~— CO (C₁-C₄ alkyl),~~

~~— SO₂ NR₂₃₅R₂₄₀,~~

~~— CO NR₂₃₅R₂₄₀,~~

~~— SO₂ (C₁-C₄ alkyl), and~~

~~— O,~~

~~wherein R₂₃₅ and R₂₄₀ at each occurrence are independently~~

~~— H, or~~

~~— C₁-C₆ alkyl,~~

~~phenyl~~

wherein each R_{245} group is ~~and R_{250} at each occurrence are~~
independently selected from the group consisting of

- H,
- (CH₂)₀₋₄CO₂C_{1-C4} alkyl
- (CH₂)₀₋₄C(=O)C_{1-C4} alkyl
- C_{1-C4} alkyl,
- C_{1-C4} hydroxyalkyl,
- C_{1-C4} alkoxy,
- C_{1-C4} haloalkoxy,
- (CH₂)₀₋₄-C_{3-C7} cycloalkyl,
- C_{2-C6} alkenyl,
- C_{2-C6} alkynyl,
- (CH₂)₀₋₄ aryl,
- (CH₂)₀₋₄ heteroaryl, and
- (CH₂)₀₋₄ heterocycloalkyl, ~~or~~

~~wherein R_{245} and R_{250} are taken together with the carbon to which they are attached to form a monocycle or bicycle of 3, 4, 5, 6, 7 or 8 carbon atoms, optionally where 1 or 2 carbon atoms is replaced by a heteroatom selected from the group consisting of~~

~~—O—~~

~~—S—~~

~~—SO₂—, and~~

~~—NR₂₂₀—;~~

wherein the aryl, heteroaryl or heterocycloalkyl group included within R_{245} and R_{250} is optionally substituted with 1, 2, or 3 groups that are independently halogen, C_{1-6} alkyl, CN or OH. \neq

~~wherein R_{255} and R_{260} at each occurrence are independently selected from the group consisting of~~

~~-H;~~

~~- C_1 - C_6 alkyl optionally substituted with 1, 2, or 3 R_{205} groups;~~

~~-(CH_2)₁₋₂-S(O)₀₋₂-(C_1 - C_6 alkyl);~~

~~-(CH_2)₀₋₄- C_3 - C_7 cycloalkyl optionally substituted with 1, 2, or 3 R_{205} groups;~~

~~-(CH_2)₀₋₄-aryl;~~

~~-(CH_2)₀₋₄-heteroaryl;~~

~~-(CH_2)₀₋₄-heterocycloalkyl;~~

~~wherein each aryl group included within R_{255} and R_{260} is optionally substituted with 1, 2, or 3 groups that are independently~~

~~R_{205} ;~~

~~R_{210} , or~~

~~C_1 - C_6 alkyl substituted with 1, 2, or 3 groups that are independently~~

~~R_{205} or~~

~~R_{210} ;~~

~~where each heteroaryl group included within R₂₅₅ and R₂₆₀ is optionally substituted with 1, 2, 3, or 4 R₂₀₀ groups, and~~

~~where each heterocycloalkyl group included within R₂₅₅ and R₂₆₀ is optionally substituted with 1, 2, 3, or 4 R₂₁₀ groups.~~

Claim 2. (original) A compound according to claim 1, wherein:

Z is aryl or heteroaryl, wherein each ring is independently optionally substituted with 1 or 2 groups independently selected from halogen, -OH, -OCF₃, -O-phenyl, -CN, -NR₁₀₀R₁₀₁, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, (CH₂)₀₋₃(C₃-C₇ cycloalkyl), aryl, heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, halogen, -OH, -CN, or -NR₁₀₀R₁₀₁.

Claim 3. (original) A compound according to claim 1, wherein X is -(C=O)-.

Claim 4. (original) A compound according to claim 1, wherein:

R₁ is -C₁-C₆ alkyl-aryl, -C₁-C₆ alkyl-heteroaryl, or -C₁-C₆ alkyl-heterocyclyl, wherein each aryl group at each occurrence is optionally substituted with 1, 2 or 3 R₅₀ groups;

wherein R₅₀ is independently selected from halogen, OH, SH, CN, -CO-(C₁-C₄ alkyl), -NR₇R₈, -S(O)₀₋₂-(C₁-C₄ alkyl), C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, or C₃-C₈ cycloalkyl;

wherein the alkyl, alkenyl, alkynyl, alkoxy, or cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁-C₄ alkyl, halogen, OH, -NR₅R₆, CN, C₁-C₄ haloalkoxy, NR₇R₈, and C₁-C₄ alkoxy;

wherein R₅ and R₆ at each occurrence are independently H or C₁-C₆ alkyl; or

wherein R₅ and R₆ and the nitrogen to which they are attached, at each occurrence form a 5 or 6 membered heterocycloalkyl ring; and

wherein R₇ and R₈ are independently selected from the group consisting of H; -C₁-C₄ alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -OH, -NH₂, and halogen; -C₃-C₆ cycloalkyl; -(C₁-C₄ alkyl)-O-(C₁-C₄ alkyl); -C₂-C₄ alkenyl; and -C₂-C₄ alkynyl;

wherein each heteroaryl at each occurrence is optionally substituted with 1 or 2 R₅₀ groups;

wherein each heterocycloalkyl group at each occurrence is optionally substituted with 1 or 2 groups that are independently R₅₀ or =O..

Claim 5. (original) A compound according to claim 1, wherein R₂ and R₃ are hydrogen.

Claim 6. (original) A compound according to claim 1, wherein R₁₅ is hydrogen.

Claim 7. (cancelled)

Claim 8. (Cancelled)

Claim 9. (original) A compound according to claim 8 wherein one of x₁, x₂, or x₃ is SO₂.

Claim 10. (original) A compound according to claim 8 wherein one of x₁, x₂, or x₃ is NH.

Claim 11. (original) A compound according to claim 8 wherein x₁, x₂, and x₃ are each CH₂.

Claim 12. (original) A compound according to claim 1 selected from the group consisting of:

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyridine-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyrazine-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1-ethyl-3-methyl-1*H*-pyrazole-5-carboxamide;

3-amino-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-1,2,4-triazole-5-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-5-methylisoxazole-3-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-6-hydroxypyridine-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-imidazole-4-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-

tetrahydronaphthalen-1-yl]amino}-2-
 hydroxypropyl)nicotinamide;
N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-
 tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-
 pyrazole-4-carboxamide;
N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-
 tetrahydronaphthalen-1-yl]amino}-2-
 hydroxypropyl)isonicotinamide;
 5-chloro-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-
 ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-
 hydroxypropyl)thiophene-2-carboxamide;
N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*S*)-6-
 neopentyl-3,4-dihydro-2*H*-chromen-4-
 yl]amino}propyl)benzamide;
N-[(1*S*,2*R*)-3-{[(4*S*)-6-tert-butoxy-3,4-dihydro-2*H*-chromen-4-
 yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;
N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*S*)-6-
 neopentyl-1,2,3,4-tetrahydroquinolin-4-
 yl]amino}propyl)benzamide;
N-[(1*S*,2*R*)-3-{[(4*S*)-6-tert-butoxy-1,2,3,4-
 tetrahydroquinolin-4-yl]amino}-1-(3,5-difluorobenzyl)-2-
 hydroxypropyl]benzamide;
N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1*S*)-7-
 neopentyl-1,2,3,4-tetrahydronaphthalen-1-
 yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(1S)-7-tert-butoxy-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4R)-6-neopentyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(4R)-6-tert-butoxy-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-neopentylphenyl)cyclohexyl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[1-(3-tert-butoxyphenyl)cyclohexyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-neopentylphenyl)cyclopropyl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[1-(3-tert-butoxyphenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4-neopentyl-1,1'-biphenyl-2-yl)methyl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(4-tert-butoxy-1,1'-biphenyl-2-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-neopentyl-9H-fluoren-9-yl)amino]propyl)benzamide;

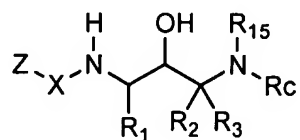
N-[(1S,2R)-3-[(2-tert-butoxy-9H-fluoren-9-yl)amino]-1-(3,5-

difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-3,5-dimethylbenzamide; and

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(4*R*)-6-ethyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide.

Claim 13. (original) A method for making a compound of formula (I)



or a pharmaceutically acceptable salt or ester thereof,
wherein Z, X, R₁, R₂, R₃, R₁₅ and R_c are as defined in claim
1.

Claim 14. (currently amended) A method for the treatment or
prevention of Alzheimer's disease, ~~mild cognitive impairment~~
~~Down's syndrome, Hereditary Cerebral Hemorrhage with Amyloidosis~~
~~of the Dutch Type, cerebral amyloid angiopathy, other~~
~~degenerative dementias, dementias of mixed vascular and~~
~~degenerative origin, dementia associated with Parkinson's~~

~~disease, dementia associated with progressive supranuclear palsy,~~
~~dementia associated with cortical basal degeneration, diffuse~~
~~Lewy body type of Alzheimer's disease~~ comprising administration
of a therapeutically effective amount of a compound or salt
according to Claim 1, to a patient in need thereof.

Claim 15. (original) A method of treatment as in claim 14,
wherein the patient is a human.

Claim 16. (cancelled)

Claim 17. (original) A pharmaceutical composition comprising a
compound according to claim 1 in combination with a
physiologically acceptable carrier or excipient.